AMENDMENTS TO THE CLAIMS

Claims 21, 23, 27, 49, 50, and 88-90 are pending in this application.

Claims 23, 88-90 are cancelled.

Claims 21, 28, and 49 are amended. After the amendments, claims 21, 27, 28, 49 and 50 will be pending.

This listing of claims replaces all prior versions and listings of claims in the application.

Claims Listing:

1.-20. (Cancelled)

21. (Currently amended) A method to detect expression of a HAS1 isoenzyme variants, wherein the HAS1 isoenzyme variant is ~~selected from the group consisting of~~ SEQ ID NO. 4~~, SEQ ID NO. 6 and SEQ ID NO. 8,~~ comprising:

i) mixing a cell or sample of cell populate from a human with reverse transcriptase in conditions enabling conversion of mRNA to DNA templates thereby generating cDNA templates;

ii) mixing said cDNA with oligonucleotide primers SEQ ID NO:9 and SEQ ID NO: 10;

a. Reacting said mixture with enzymes and compounds to enable specific fragments of DNA to be increased in number;

b. Detecting the presence of an increased number of resulting DNA fragments of particular size associated with the presence of ~~particular HAS1 isoenzyme variants~~ SEQ ID NO:3.

22. (Cancelled)

23. (Cancelled)

24. (Withdrawn) The method of claim 21 wherein the isoenzyme variant is HAS1Vb.

25. (Withdrawn) The method of claim 21 wherein the isoenzyme variant is HAS1Vc.

26. (Withdrawn) The method of claim 21 wherein the isoenzyme is HAS2.

27. (Previously presented) The method of claim 21 wherein the process is performed using a microfluidic device.

28. (Currently amended) A method to detect expression of HAS1Va isoenzyme variant in a cell or cell population comprising detection of single nucleotide conversion of base 924 of SEQ ID NO:3 ~~the HAS1Va cDNA~~ from a cytosine to a thymidine residue.

29 - 48. (Cancelled)

49. (Currently amended) A method to determine the likelihood of poor clinical outcome in a human suffering from multiple myeloma comprising characterizing HAS isoenzyme variant expression in a cell or cell population using the method of claim 21, wherein the HAS isoenzyme variant is ~~selected from the group consisting of~~ SEQ ID NO. 4~~, SEQ ID NO. 6 and SEQ ID NO. 8~~.

50. (Previously presented) The method of claim 49 wherein the cell or cell population is selected from the group comprising blood, B-cells, CD 19.sup.+ B cells, CD 19.sup.+ peripheral blood mononuclear cells and bone marrow plasma cells.

51. (Withdrawn) An isolated and purified DNA molecule comprising a DNA segment encoding a human hyaluronan synthase variant or enzymatically active fragment thereof, wherein the DNA molecule hybridizes under stringent conditions to SEQ ID NO:3 or compliment thereof.

52. (Withdrawn) The DNA molecule of claim 51 wherein the DNA segment encodes the human hyaluronan synthase isoenzyme variant HAS1Va.

53. (Withdrawn) The DNA molecule of claim 51 wherein the DNA segment encodes a hyaluronan synthase having SEQ ID NO: 4.

54. (Withdrawn) An isolated and purified DNA molecule comprising a DNA segment encoding a human hyaluronan synthase variant or enzymatically active fragment thereof, wherein the DNA molecule hybridizes under stringent conditions to SEQ ID NO:5 or compliment thereof.

55. (Withdrawn) The DNA molecule of claim 54 wherein the DNA segment encodes the human hyaluronan synthase isoenzyme variant HAS1Vb.

56. (Withdrawn) The DNA molecule of claim 54 wherein the DNA segment encodes a hyaluronan synthase having SEQ ID NO: 6.

57. (Withdrawn) An isolated and purified DNA molecule comprising a DNA segment encoding a human hyaluronan synthase variant or enzymatically active fragment thereof, wherein the DNA molecule hybridizes under stringent conditions to SEQ ID NO:7 or compliment thereof.

58. (Withdrawn) The DNA molecule of claim 57 wherein the DNA segment encodes the human hyaluronan synthase isoenzyme variant HAS1Vc.

59. (Withdrawn) The DNA molecule of claim 57 wherein the DNA segment encodes a hyaluronan synthase having SEQ ID NO: 8.

60. (Withdrawn) An isolated and purified DNA molecule comprising a DNA segment capable of selectively binding to the mRNA of human hyaluronan synthase isoenzyme-1 (HAS1) or nucleotide product thereof; allowing, when used in conjunction with a corresponding downstream DNA segment capable of selectively binding to mRNA of human hyaluronan synthase isoenzyme-1 (HAS1) or nucleotide product thereof; DNA

fragment amplification and identification of HAS1 isoenzyme variants, wherein the DNA molecule hybridizes under stringent conditions to SEQ ID NO:9.

61. (Withdrawn) An isolated and purified DNA molecule comprising a DNA segment capable of selectively binding to the mRNA of human hyaluronan synthase isoenzyme-1 (HAS1), or nucleotide product thereof; allowing, when used in conjunction with a corresponding downstream DNA segment capable of selectively binding to mRNA of human hyaluronan synthase isoenzyme-1 (HAS1), or nucleotide product thereof; DNA fragment amplification and identification of HAS1 isoenzyme variants, wherein the DNA molecule hybridizes under stringent conditions to SEQ ID NO:10.

62. (Withdrawn) A method to treat a patient experiencing disease comprising: i) characterizing HAS1 isoenzyme variant expression in a cell or cell population; ii) evaluating aberrant HAS1 isoenzyme variant expression; and iii) administering compounds to the cell or cell population resulting in diminished HAS1 isoenzyme variant activity.

63. (Withdrawn) The method of claim 62 wherein HAS isoenzyme activity is diminished through decreased mRNA translation.

64. (Withdrawn) The method of claim 62 wherein mRNA translation is decreased through administration of agents that selectively bind to HAS isoenzyme variant mRNA.

65. (Withdrawn) The method of claim 64 wherein the agent is anti-sense RNA.

66. (Withdrawn) The method of claim 64 wherein the agent is anti-sense DNA.

67. (Withdrawn) The method of claim 64 wherein the agent is small inhibitory RNA.

68. (Withdrawn) The method of claim 62 wherein the HAS1 isoenzyme variant activity is diminished through decreased activity of the HAS1 isoenzyme variant protein.

69. (Withdrawn) The method of claim 68 wherein protein activity is decreased through administration of an agent which selectively binds to HAS1 isoenzyme variants.

70. (Withdrawn) The method of claim 69 wherein the agent is a peptide.

71. (Withdrawn) The method of claim 70 wherein the agent is an antibody.

72. (Withdrawn) The method of claim 70 wherein the agent is an antibody fragment.

73. (Withdrawn) The method of claim 68 wherein the agent is vesnarinone.

74. (Withdrawn) The method of claim 68 wherein the agent is hyaluronic acid.

75. (Withdrawn) A method to treat a patient susceptible to disease comprising: i) characterizing HAS1 isoenzyme variant expression in a cell or cell population; Evaluation of aberrant HAS1 isoenzyme variant expression; and ii) administering at least one compound to the cell or cell population resulting in diminished HAS1 isoenzyme variant activity.

76. (Withdrawn) The method of claim 75 wherein HAS isoenzyme activity is diminished through decreased mRNA translation.

77. (Withdrawn) The method of claim 76 wherein mRNA translation is decreased through administration of at least one agent that selectively binds to HAS isoenzyme variant mRNA.

78. (Withdrawn) The method of claim 77 wherein the agent is anti-sense RNA.

79. (Withdrawn) The method of claim 77 wherein the agent is anti-sense DNA.

80. (Withdrawn) The method of claim 77 wherein the agent is small inhibitory RNA.

81. (Withdrawn) The method of claim 75 wherein the HAS1 isoenzyme variant activity is diminished through decreased activity of the HAS1 isoenzyme variant protein.

82. (Withdrawn) The method of claim 81 wherein protein activity is decreased through administration of an agent which selectively binds to HAS1 isoenzyme variants.

83. (Withdrawn) The method of claim 82 wherein the agent is a peptide.

84. (Withdrawn) The method of claim 83 wherein the agent is an antibody.

85. (Withdrawn) The method of claim 83 wherein the agent is an antibody fragment.

86. (Withdrawn) The method of claim 83 wherein the agent is vesnarinone.

87. (Withdrawn) The method of claim 83 wherein the agent is hyaluronic acid.

88. (Cancelled) A method to monitor malignant cells in a human comprising detection of HAS isoenzyme variants in a sample of cells or cell populate from a human, wherein the HAS isoenzyme variants are selected from the group consisting of SEQ ID NO. 4, SEQ ID NO. 6 and SEQ ID NO. 8.

89. (Cancelled) The method of claim 88 wherein the human is suffering from Multiple Myeloma.

90. (Cancelled) The method of claim 88 wherein the human is suffering from Waldenstrom's Macroglomulemia.

91. (Withdrawn) A kit for characterizing HAS isoenzyme or isoenzyme variant expression in a cell or cell population comprising: i) the DNA of claims 51, 54, 57 or 60, ii) compounds and enzymes sufficient to enable specific fragments of DNA to be increased in number, and iii) instructions enabling one to amplify and identify HAS isoenzyme or isoenzyme variant specific fragments.

92. (Withdrawn) The kit of claim 91 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to monitor previously diagnosed Waldenstrom's Macroglomulemia.

93. (Withdrawn) The kit of claim 91 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to monitor previously diagnosed Multiple Myeloma.

94. (Withdrawn) The kit of claim 91 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to diagnose Multiple Myeloma.

95. (Withdrawn) The kit of claim 91 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to assess clinical outcome of Multiple Myeloma patients.

96. (Withdrawn) A kit for characterizing HAS isoenzyme variant expression in a cell or cell population comprising nucleotides capable of binding selectively to, and thereby distinguishing, HAS isoenzyme or isoenzyme variant transcripts; compounds sufficient to enable formation and identification of complex formed between the nucleotides and HAS isoenzyme variant transcripts; and instructions enabling one to identify HAS isoenzyme variant expression.

97. (Withdrawn) The kit of claim 96 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to monitor previously diagnosed Waldenstrom's Macroglomulemia.

98. (Withdrawn) The kit of claim 96 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to monitor previously diagnosed Multiple Myeloma.

99. (Withdrawn) The kit of claim 96 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to diagnose Multiple Myeloma.

100. (Withdrawn) The kit of claim 96 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to assess clinical outcome of Multiple Myeloma patients.

101. (Withdrawn) A kit for characterizing HAS isoenzyme or isoenzyme variant expression in a cell or cell population comprising peptides capable of binding selectively to, and thereby distinguishing, HAS isoenzyme or isoenzyme variant proteins; compounds sufficient to enable formation and identification of complex formed between the complex formed between the peptide and HAS isoenzyme or isoenzyme variant protein; and instructions enabling one to identify HAS isoenzyme or isoenzyme variant proteins.

102. (Withdrawn) The kit of claim 101 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to monitor previously diagnosed Waldenstrom's Macroglomulemia.

103. (Withdrawn) The kit of claim 101 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to monitor previously diagnosed Multiple Myeloma.

104. (Withdrawn) The kit of claim 101 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to diagnose Multiple Myeloma.

105. (Withdrawn) The kit of claim 101 wherein characterizing HAS isoenzyme or isoenzyme variant expression is used to assess clinical outcome of Multiple Myeloma patients.

106 - 107. (Cancelled)